1187 Thrombolytic Therapy for Acute Myocardial Infarction: Clinical Aspects

Wednesday, April 1, 1998, Noon–2:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 1:00 p.m.–2:00 p.m.

1187-149 Does IV Heparin After Streptokinase Prevent Left Ventricular Thrombus in Acute Anterior Myocardial Infarction?: A Randomised, Prospective, Double Blind, Placebo Controlled Study

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Left Ventricular Thrombus (LVT) is a relatively common and potentially serious complication of Acute Anterior Myocardial Infarction (AAMI). The value of heparin in preventing LVT is controversial. We randomised 150 patients with first AMI who received Streptokinase (SK) to either I.V heparin (HEP, N = 78) or Placebo (PLA, N = 72) for 4 days. All patients had echocardiography to assess the presence of a "definitive" LVT before discharge (5 ± 1.3 days). APTT was kept 3–4 times control in HEP group, and 300 mg Aspirin was given daily to all patients.

The two groups were well matched. There was no significant difference in the peak CPK (3000 ± 2140 in HEP group vs 3100 ± 2070 in PLA group, p = N.S), or in pre-SK fibrinogen (3.0 ± 1.02g% in HEP group vs 2.86 ± 0.88 in PLA group, p = N.S). Both groups showed a dramatic fall in fibrinogen level post-SK to (0.7 ± 0.4 g% and 0.68 ± 0.47 g%, p < 0.001, p < 0.001 respectively).

LVT was found in 13/78 patients who received heparin (16.6%) vs 10/72 in PLA group (13.8%), [p = NS, chi-square test]. When the whole group (N = 150) was analyzed regardless to heparin status, it was found that those with LVT had a higher peak CPK (3662 ± 2237 U/ml) than those without LVT (2954 ± 2050 U/ml)

Conclusion: I.V heparin after SK does not prevent LV thrombus formation in AAMI, in fact there was a slight tendency towards higher incidence in the heparin group. LV thrombus seems to be related more to the size of infarction than to the administration of heparin. A different agent may have to be tried.

1187-150 Activation of the Contact Pathway in Patients Treated With t-PA or Streptokinase may Attenuate Clot Lysis

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Background: We have shown that activation of the contact system is a potential mechanism for increases in thrombin activity in patients treated with streptokinase (SK) or t-PA. Because thrombin activates plasma procarboxypeptidase-B (thrombin-activated fibrinolysis inhibitor) that acts to attenuate clot lysis, contact activation may limit the efficacy of thrombolysis.

Methods/Results: We measured XIIa concentrations with a novel enzyme-linked immunosorbent assay based on a specific monoclonal antibody in patients treated with 1,500,000 U SK (n = 15) or 100 mg t-PA (n = 12). Sixty minutes after initiation of the lytic agents, factor XIIa increased from 3.2 ± 0.5 to 6.9 ± 0.8 ng/ml with SK (p = 0.0002), and from 2.5 ± 0.2 to 6.8 ± 0.9 ng/ml with t-PA (p = 0.0003). Increases in factor XIIa were also induced in vitro by incubation of of SK (250 U/ml) or t-PA (5 ng/ml) with recalcified citrated plasma. The rate of plasma clot lysis induced by 250 U/ml of SK in recalcified citrated plasma was accelerated by 205 ± 80% with 1 μM hirudin and 172 ± 144% with 2.5 μM corn trypsin inhibitor (CTI[a specific factor XIIa inhibitor]) (p < 0.01 vs no inhibitor). Acceleration with 2.5 ng/ml t-PA was 64 ± 26% with hirudin and 40 ± 31% with CTI (p < 0.01). Inhibition of plasma carboxypeptidase activity with a synthetic inhibitor also accelerated clot lysis with SK by 189 ± 128%, and 67 ± 33% with t-PA (p < 0.01 for both, compared with no inhibitor).

Conclusion: Marked factor XII-dependent activation of the contact system of coagulation occurs in patients treated with fibrinolytic agents, likely secondary to direct activation of factor XII by plasmin, as previously reported. Increases in thrombin activity in response to thrombolysis may attenuate the rate of clot lysis because of the rapid thrombin-mediated increase in plasma carboxypeptidase activity.

1187-151 One-Year Clinical Follow-up of Patients With Inferior Acute Myocardial Infarction and Anterior ST Depression. Results of a Randomized Trial of Primary Angioplasty Versus Accelerated Tissue Plasminogen Activator

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Primary (P) PTCA is a logistically demanding therapeutic option; identification of AMI patients (pts) in whom P-PTCA is most beneficial is important to optimize both AMI treatment and P-PTCA use. Anterior ST depression (ASTD) in inferior AMI is a marker of poor prognosis, but little is known about the long-term outcome of P-PTCA and t-PA in these pts. One-month results from our study in 110 pts randomized to either treatment showed advantages of P-PTCA as to new target vessel revascularization (TVR) (3.6% vs 25.5%, p = 0.003), left ventricular ejection fraction (LVEF) (55% vs 48%, p = 0.0001), TIMI 3 flow at discharge (100% vs 59%, p < 0.0001), and hospital stay (9.2 vs 12 days, p = 0.0001), although combined mortality and re-AMI were not significantly different (3.6 vs 11%, p = ns).

We present the long-term results on mortality and non-fatal re-AMI, need for TVR, and hospital readmission on all 106 pts discharged alive after randomized treatment with P-PTCA (54 pts) and accelerated t-PA (52 pts), 50% of pts of each group had multi-vessel disease. At a mean follow-up of 18.2 ± 9.7 months no difference was observed in terms of mortality and re-AMI (1.8% vs 1.3%, p = ns). The need for TVR was lower in the P-PTCA group (1.8% vs 17%, p = 0.01), as was the incidence of new hospital admissions (5.5% vs 40%, p = 0.0001). Using Kaplan-Meier curves for event-free analysis (non-ischemic cardiac events and elective revascularization were included in the analysis), patients randomly assigned to P-PTCA had a significantly better event-free survival (log. rank 16.2, p < 0.0001), with no difference in mortality (log. rank 1.4, p = ns).

Conclusion: superior results in pts randomized to P-PTCA, as seen at one-month persist at long-term, with fewer TVR and hospital readmissions. Mortality and reinfarction rates remain equivalent with either treatment at long-term follow-up; this is probably the effect of the high rate of reperfusion obtained by both treatments in our cohort of pts, as reflected by a preserved LVEF at discharge, and of extensive subsequent use of new revascularization procedures (both urgent and elective), specially in pts with initial thrombolysis.

1187-152 Bedside Lytic Activity Assessment During Accelerated tPA and TNK-tPA Therapy for Acute Myocardial Infarction

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Background: Accelerated infusion of tPA (Acc tPA) is considered as the most effective thrombolytic regimen in AMI (Gusto I trial). TNK-tPA is a new tPA mutant suggested to be more fibrin specific, more resistant to PAI-1, and of longer half-life given as a single IV bolus under clinical evaluation.

Methods: To compare the lytic activity (L Act) induced by Acc tPA and TNK-tPA (30 or 40 mg), lysis onset time (LOT) of a fresh autologous thrombus was determined ex-vivo using a bedside thrombolytic assessment system (TAS™, CVDI, USA) at baseline, 10, 60, 90 and 180 min in 80 AMI pts, 61 treated with Acc tPA and 19 with TNK-tPA. L Act is proportionate to shortening of LOT, absent when LOT > 1200 sec. The lytic reserve (LR) was assessed by the LOT response to 1000 U/ml tPA in vitro at baseline and 180 min.

Results: LOT determinations are expressed as median (in seconds):

		Baseline	10 min	60 min	90 min	180 min
LOT-	tPA	>1200	138	–	169	>1200
L Act	TNK-tPA	>1200	111*	192	328*	1139**
LOT-	tPA	103	–	–	–	116*
LR	TNK-tPA	118	–	–	–	121

*p < 0.0001, **p = 0.045 vs tPA, *p < 0.012 vs baseline

Conclusions: 1) The TNK-tPA bolus (30 or 40 mg) induces a more intense immediate lytic response than 15 mg tPA bolus. This activity weans gradually keeping some L Act at 3 hours, by contrast the tPA infusion maintains the established L Act (with the same intensity) for 90 rain followed by rapid weaning leaving no activity at 3 hours. 2) Unlike tPA, TNK-tPA does not impaire the lytic reserve reflecting further enhancement of fibrin specificity.